Claims 21, 22, 24-33 and 35-41 were rejected for allegedly lacking enablement other than for claims limited to sarcotoxin 1a. Claims 21-41 were rejected for allegedly being indefinite.

Support for the Amendments

Support for the amendments can be found through out the specification, claims, and drawings, as originally filed. For example, claims 23, 24, 25, 29, 30, 31, 34, 35, 38, 39, 40 and 41 are amended to improve or to correct grammar. Claims 21 and 32 were amended to clarify a reference point for enhanced fungal resistance in transgenic plants. Support for new claims 42-47 can be found in, *e.g.*, the originally filed claims. No new matter has been introduced.

Telephone Interview

Applicants' representative greatly appreciates the courtesy shown by Examiner Nelson in the August 9, 2000 telephone interview and further appreciates the Examiner's careful consideration of the arguments made during the interview.

Objections

Claims 31, 40 and 41 were objected for minor informalities. Applicants have amended the claims by incorporating the suggestions provided by the Examiner. Accordingly, the objections of the claims are now moot.

Rejections under Sec. 112, 1st paragraph

A. Written Description

Claims 21, 22, 24-33 and 35-41 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention. According to page 3 of the Office Action, Applicants only describe a single anti-bacterial gene from a Diptera insect. The Office Action also states that Applicants must describe a representative number of species of the claimed genus (*i.e.*, anti-bacterial genes from a Diptera insect), or must describe structural features which are characteristic of most of the species of the claimed genus.

Applicants respectfully traverse this rejection. As noted in the previous Amendments, the standards set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) are not applicable to the present application. Applicants again note that the claimed invention is not directed at any particular sequences or nucleic acids. Rather, the claims are directed to new methods and plants that contain anti-bacterial peptide sequences from a Diptera insect to confer fungal resistance. In fact, a number of anti-bacterial peptide sequences from a Diptera insect were well-known in the art at the time of the present application as described in detail below. Therefore, the facts of the present application are not analogous to the facts of *University of California*, and the standards set forth in *University of California* are not applicable to the present application.

In the present application, a number of anti-bacterial sequences from a Diptera insect were well-known in the art, and such well-known information need not be explicitly described in the specification. For example, the full length amino acid sequences of sarcotoxin 1b, 1c and 1d are described in, *e.g.*, Figure 5 of Okada & Natori, *J. Biol. Chem.* 260(12):7174-7177 (1985) and Figure 7 of Matsuyama, *J. Biol. Chem.* 263(32):17112-17116 (1988). The full length amino acid and nucleic acid sequences of cecropins A, B and D are described in, *e.g.*, Figure 2 of Kylsten *et al.*, *EMBO J.* 9(1):217-214 (1990); and Figures 1 and 2 of Rosetto *et al.*, *Gene* 134(2):241-243 (1993). The full length amino acid sequence of sapecin is described in, *e.g.*, Figure 1 of Yamada & Natori, *Biochem. J.* 298:623-628 (1994). Therefore, a representative number of anti-bacterial sequences from a Diptera insect were well-known in the art at the time of the invention. In view of these facts, one of skill in the art could have identified any one of these or other anti-bacterial peptides from a Diptera insect for use in the present application. Accordingly, withdrawal of the rejection is respectfully requested.

B. Enablement

Claims 21, 22, 24-33 and 35-41 were rejected under 35 U.S.C. §112, first paragraph, for allegedly enabling only for claims limited to methods of enhancing fungal resistance with, and transgenc plants comprising, the sarcotoxin 1a gene. According to page 5 of the Office Action, Applicants disclose a single DNA sequence (*i.e.*, sarcotoxin 1a gene) and do not disclose other DNA sequences encoding anti-bacterial peptide from a Diptera insect or how to isolate these DNA sequences. The Office Action further invites Applicants to provide

evidence of availability of other anti-bacterial peptide sequences which are functionally and structurally related to the disclosed sarcotoxin 1a.

Applicants respectfully traverse this rejection. The proper test of enablement is "whether one skilled in the art could make or use the claimed invention from the disclosure in the patent coupled with information known in the art without undue experimentation." *United States v. Teletronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). MPEP §2164.01. Applicants submit that a number of anti-bacterial peptide sequences from a Diptera insect, other than sarcotoxin 1a, were well-known in the art at the time of the invention. Their sequence information and their structural relationship to sarcotoxin 1a are described in detail below.

1. Sarcotoxin 1b, 1c, and 1d

Sarcotoxin 1b, 1c, and 1d, which are members of the sarcotoxin 1 family, were known in the art prior to the effective filing date (*See* Okada & Natori, *supra*; and Matsuyama & Natori, *supra*, page 17115, left column, lines 31-42). Their full length peptide sequences were also known in the art (*See, e.g.*, Figure 5 of Okada & Natori and Figure 7 of Matsuyama & Natori). Moreover, it was known that these peptides had almost identical structural properties with sarcotoxin 1a (*see, e.g.*, Okada & Natori, *supra*, page 7175, right column, lines 25-27; and Matsuyama & Natori, *supra*, page 17115, Fig. 7). For example, these peptides consist of 39 amino acid residues and differ in only 2-3 amino acid residues. These peptides are structurally so similar to the point where they could not be separated by polyacrylamide gel electrophoresis (Okada & Natori, *supra*, page 7175, right column, lines 40-44)). It was also known that they share functional properties with sarcotoxin 1a (*see, e.g.*, Okada & Natori, *supra*, page 7175, Fig. 2, and page 7176, left column, lines 23-28). In view of these facts known in the art and the present disclosure, one of skill in the art would have known that these peptides, instead of sarcotoxin 1a, could have been used to transform a plant of the present application to confer fungal resistance.

2. Cecropin A, B and D

Cecropin A, B and D from Diptera insect, which are homologues of sarcotoxin 1, were known in the art prior to the effective filing date (*see, e.g.*, Kylsten *et al.*, *supra*; and

Rosetto *et al.*, *supra*). The amino acid sequences of these cecropin share extremely high homology with those of sarcotoxin 1. Therefore, those skilled in the art predicted that they would share functional activity based on their homology (*see, e.g.*, Okada & Natori, *supra*, page 7176, right column, lines 7-15). In fact, it was later shown that cecropin also has antifungal activity (*see, e.g.*, DeLucca *et al., supra*, page 482, left column, lines 6-14). In view of these facts known in the art and the present disclosure, one of skill in the art would have known that these cecropin peptides, instead of sarcotoxin 1a, could have been used to transform a plant of the present application to confer fungal resistance.

3. Sapecin

Sapecin was known as a potent antibacterial protein of *Sarcophaga peregrina* (flesh fly). Although sapecin was known to have antibacterial activity mainly against Gram-positive bacteria, it was also known that a hendecapeptide derived from sapecin had antifungal activity (*see, e.g.*, Yamada & Natori, *supra*, page 624, right column, line 37 to page 625, left column, line 14). Yamada & Natori also describes that the analogues of this hendecapeptide substituted by hydrophobic and/or basic amino acids had enhanced antifungal activity as well as antibacterial activity (*see* page 627, right column, lines 1-13). In view of these facts known in the art and the present disclosure, those skilled in the art would have known that these peptides, instead of sarcotoxin 1a, could have been used to transform a plant of the present application to confer fungal resistance.

At page 5 of the Office Action, in response to Applicants' arguments that a number of anti-bacterial peptides from a Diptera insect were well-known in the art, the Examiner responds that "the instant invention deploys DNA sequences, not peptides." In view of this statement, it may be the position of the Examiner that availability of peptide sequences is not sufficient and that DNA sequences must be available to practice the claimed invention without undue experimentation.

Applicants respectfully traverse. The anti-bacterial peptides from a Diptera insect are relatively short. For example, the full length sarcotoxin 1b, 1c and 1d are only 39 amino acid residues. Moreover, amino acid sequences of these and other full length anti-

bacterial peptides were available at the time of the present invention. *Assuming arguendo* that DNA sequences of some of these anti-bacteria peptides were not available at the time of the present invention, Applicants respectfully submit that one of ordinary skill in the art would have been able to produce DNA sequences that encode these relatively short peptides without undue experimentation. For example, a DNA sequence could have been artificially synthesized based on degenerate codons of amino acid residues of these peptides. Accordingly, one of ordinary skill in the art would have been able to transform a plant with a number of DNA sequences encoding anti-bacterial peptides from a Diptera insect to confer fungal resistance without undue experimentation.

In summary, there were many antibacterial peptides that could be used in the present invention before the filing of the present application. However, prior to the Applicants' invention, the production of a fungi-resistant plant by using such antibacterial peptides was not known. Based on the teachings of the present application, those skilled in the art would have been able to confer resistance to pathogenic fungi on a plant using various antibacterial peptides from a Diptera insect, other than sarcotoxin 1a, without undue experimentation. Therefore, the Examiner's requirement to limit the scope of the claims to sarcotoxin 1a is unduly restrictive. Accordingly, withdrawal of the rejection is respectfully requested.

Rejections under Sec. 112, 2nd paragraph

Claims 21-41 were rejected for allegedly being indefinite for a lack of proper antecedent basis or for minor grammatical errors. Applicants have amended the claims by incorporating the Examiner's suggestions. These amendments do not narrow or alter the scope of the claims in any way. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

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APPENDIX I

21. A method of conferring resistance to pathogenic fungi on a plant using a DNA sequence encoding an anti-bacterial peptide from a Diptera insect, the method comprising the steps of: transforming a plant cell by introducing the DNA sequence encoding the anti-bacterial peptide from the Diptera insect; and regenerating the transformed plant cell into a transgenic plant expressing the anti-bacterial peptide, wherein the transgenic plant has enhanced resistance to pathogenic fungi as compared to the plant before transformation.

22. The method according to claim 21, wherein the pathogenic fungi are *Rhizoctonia solani, Pythium aphanidermatum, and Phytophthora infestans.*

23. The method according to claim 21, wherein the anti-bacterial peptide from the Diptera insect is sarcotoxin 1a.

24. The method according to claim 21, wherein the DNA sequence encoding the anti-bacterial peptide from the Diptera insect is in an expression vector, said expression vector comprising an expression cassette comprising the DNA sequence encoding the anti-bacterial peptide from the Diptera insect operably linked to a first plant promoter and a drug resistance gene operably linked to a second plant promoter which is constitutively expressed, wherein the first plant promoter and the second plant promoter are positioned adjacent to each other.

25. The method according to claim 21, wherein the DNA sequence encoding the anti-bacterial peptide from the Diptera insect is operably linked to a plant gene via the hinge region of a tobacco chitinasa gene.

26. The method according to claim 21, wherein the DNA sequence encoding the anti-bacterial peptide from the Diptera insect is operably linked to a signal sequence from a plant gene.

27. The method according to claim 24, wherein the first plant promoter is an inducible promoter.

28. The method according to claim 27, wherein the inducible promoter is a promoter induced by stress.

29. The method according to claim 28, wherein the promoter induced by stress is the promoter of the tobacco PR-1a gene.

30. The method according to claim 24, wherein the expression cassette further comprises the terminator of the tobacco PR-1a gene operably linked downstream of the DNA sequence encoding the antibacterial peptide from the Diptera insect.

31. The method according to claim 24, wherein the second plant promoter is the cauliflower mosaic virus 35S promoter.

32. A plant which confers resistance to pathogenic fungi, the plant comprising an expression vector comprising an expression cassette comprising a DNA sequence encoding an anti-bacterial peptide from a Diptera insect operably linked to an inducible promoter and a drug resistance gene operably linked to a constitutively expressed promoter, wherein the inducible promoter and the constitutively expressed promoter are positioned adjacent to each other, wherein the transgenic plant has enhanced resistance to pathogenic fungi as compared to the plant before transformation.

33. The plant according to claim 32, wherein the pathogenic fungi are *Rhizoctonia solani*, *Pythium aphanidermatum*, and *Phytophthora infestans.*

34. The plant according to claim 32, wherein the anti-bacterial peptide from the Diptera insect is sarcotoxin 1a.

35. The plant according to claim 32, wherein the DNA sequence encoding the anti-bacterial peptide from the Diptera insect is operably linked to a plant gene via the hinge region of a tobacco chitinase gene.

36. The plant according to claim 32, wherein the DNA sequence encoding the anti-bacterial peptide from the Diptera insect is operably linked to a signal sequence from a plant gene.

37. The plant according to claim 32, wherein the inducible promoter is a promoter induced by stress.

38. The plant according to claim 37, wherein the promoter induced by stress is the promoter of the tobacco PR-1a gene.

39. The plant according to claim 32, wherein the expression cassette further comprises the terminator of the tobacco PR-1a gene operably linked downstream of the DNA sequence encoding the anti-bacterial peptide from the Diptera insect.

40. The plant according to claim 32, wherein the constitutively expressed promoter is the cauliflower mosaic virus 35S promoter.

41. The plant according to claim 32, wherein the expression vector further comprises a T-DNA region and a drug resistance gene.

42. The method according to claim 21, wherein the anti-bacterial peptide from Diptera insect is selected from the group consisting of members of the sarcotoxin 1 family and homolog thereof, and peptides derived from sapecin.

43. The method according to claim 21, wherein the anti-bacterial peptide from Diptera insect is selected from the group consisting of members of the sarcotoxin 1 family and homolog thereof.

44. The method according to claim 21, wherein the anti-bacterial peptide from Diptera insect is selected from members of the sarcotoxin 1 family.

45. The plant according to claim 32, wherein the anti-bacterial peptide from Diptera insect is selected from the group consisting of members of the sarcotoxin 1 family and homolog thereof, and peptides derived from sapecin.

46. The plant according to claim 32, wherein the anti-bacterial peptide from Diptera insect is selected from the group consisting of members of the sarcotoxin 1 family and homolog thereof.

47. The plant according to claim 32, wherein the anti-bacterial peptide from Diptera insect is selected from members of the sarcotoxin 1 family.